# Cell Specific Pallidal Control of the Cortical Striatal Pathway

Shubhi Verma

# Outline

- Background
- Materials and Methods
- Data
- Analyses
- Discussion
- Acknowledgements

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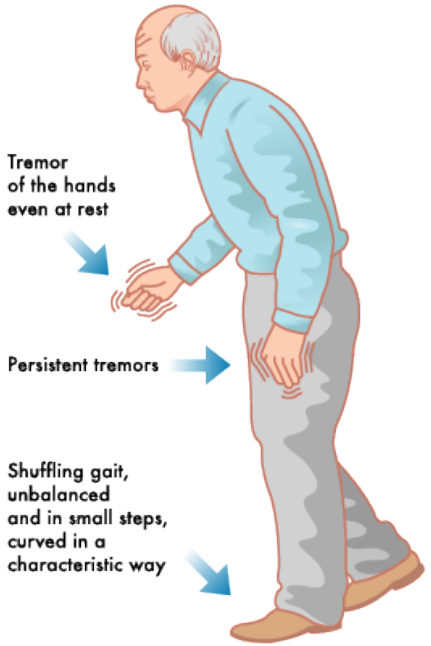
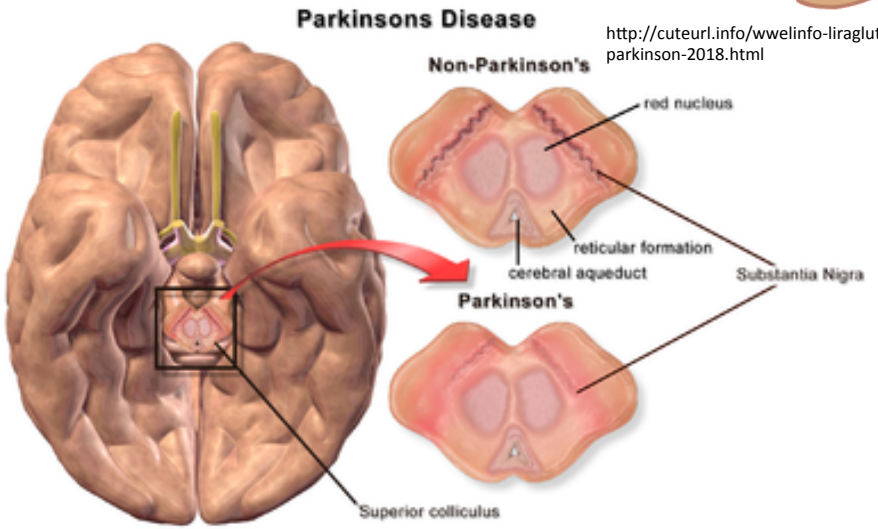
# Parkinson's Disease

- A neurodegenerative disease of the basal ganglia
- Caused by dopamine depletion (DeMaagd & Philip, 2015)
- 1-3% of people older than 80 years old (DeMaagd & Philip, 2015)
- Symptoms
  - Tremors
  - Muscular rigidity
  - Bradykinesia
  - Dementia




http://cuteurl.info/wwelinfo-liraglutide-parkinson-2018.html




https://en.wikipedia.org/wiki/Pathophysiology_of_Parkinson%27s_disease

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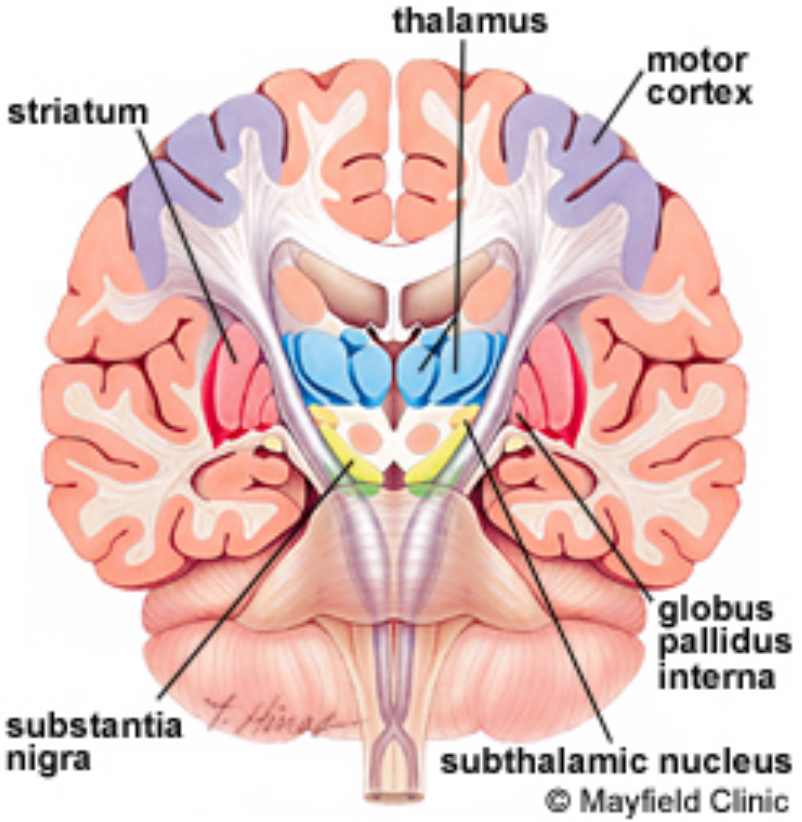
# The Basal Ganglia

- Basal Ganglia
  - A collection of nuclei
    - Substantia Nigra
    - Subthalamic Nucleus
    - External Globus Pallidus
    - Striatum
- Areas of interest
  - Striatum
  - External Globus Pallidus




https://www.mayfieldclinic.com/PE-PD.htm

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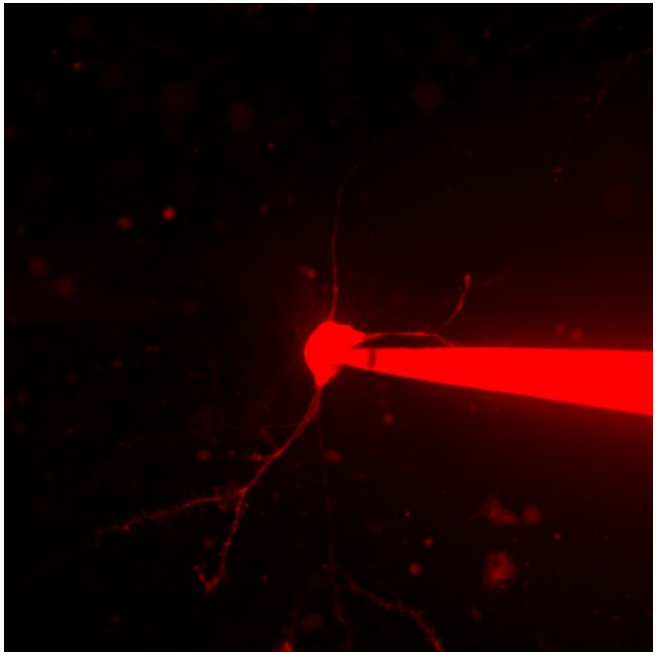
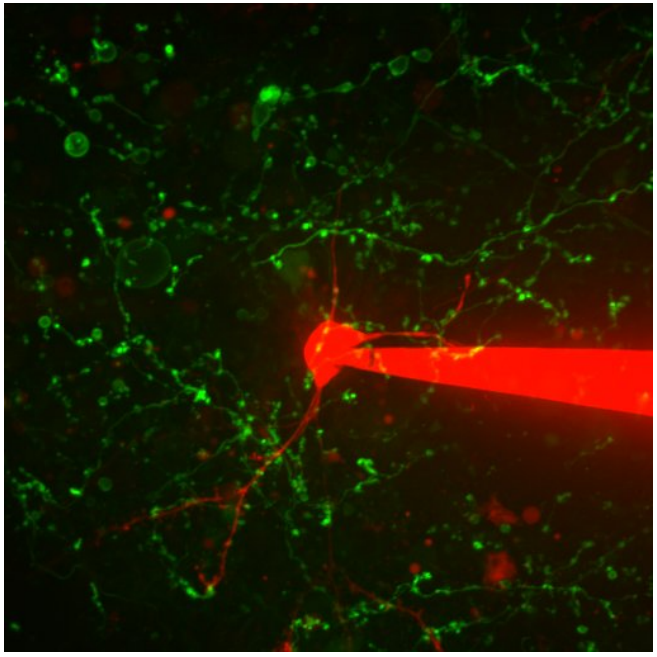
# Spiny Projection Neurons

- Neurons of the Striatum (Surmeier et al., 2007)
- Sometimes referred to as Medium Spiny Neurons
- Two main classes of receptors: D1 and D2 receptors (Surmeier et al., 2007)
- Direct and Indirect SPNs





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# Pallidostriatal Pathway

- Striatal input to GPe is inhibitory (Jaeger et al., 2011)
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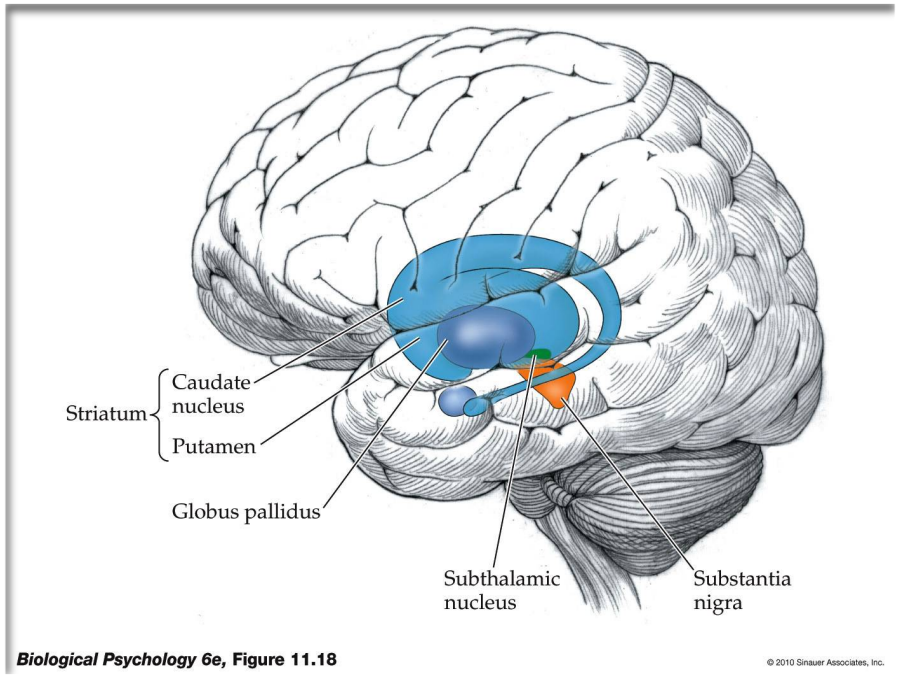
- Npas1+ GPe neurons project to the Str (Hernandez et al., 2016)




https://beyondthedish.wordpress.com/tag/striatum/

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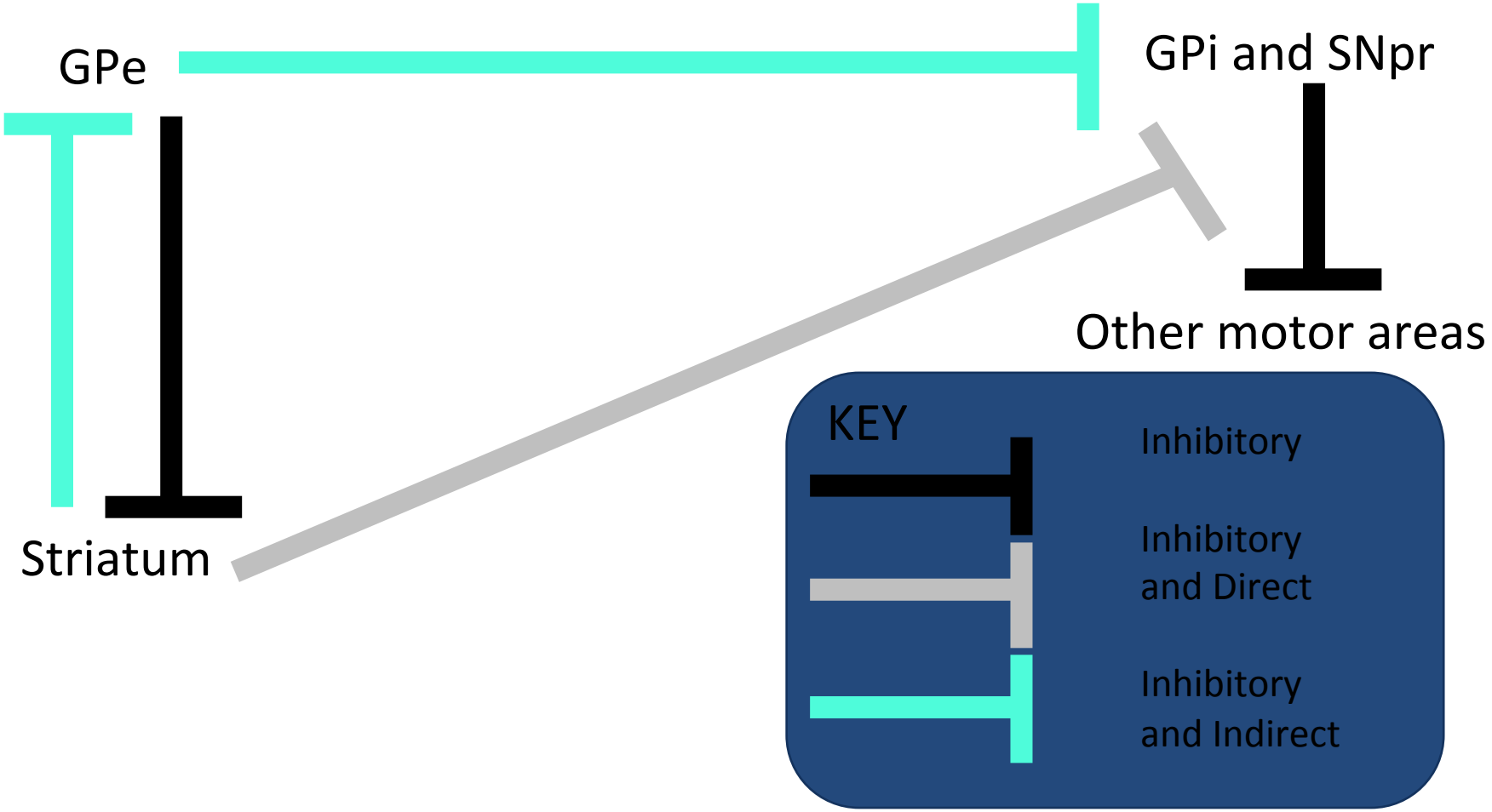
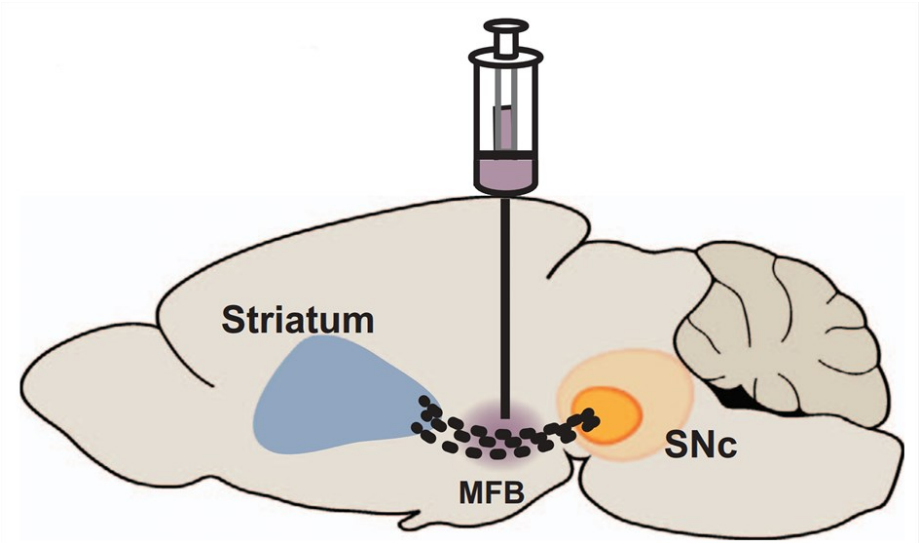
# Striatal and Pallidal Pathways



# Materials and Methods

- Parkinsonian Mice
  - Symptoms produced using 6-hydroxydopamine (6-OHDA)
  - 6-OHDA injected into the brain
  - Destroys dopaminergic neurons of the substantia nigra
  - Induces symptoms of Parkinson's Disease




https://www.creative-biolabs.com/drug-discovery/therapeutics/6-ohda-unilateral-lesion-rat-model-of-parkinson-s-disease.htm

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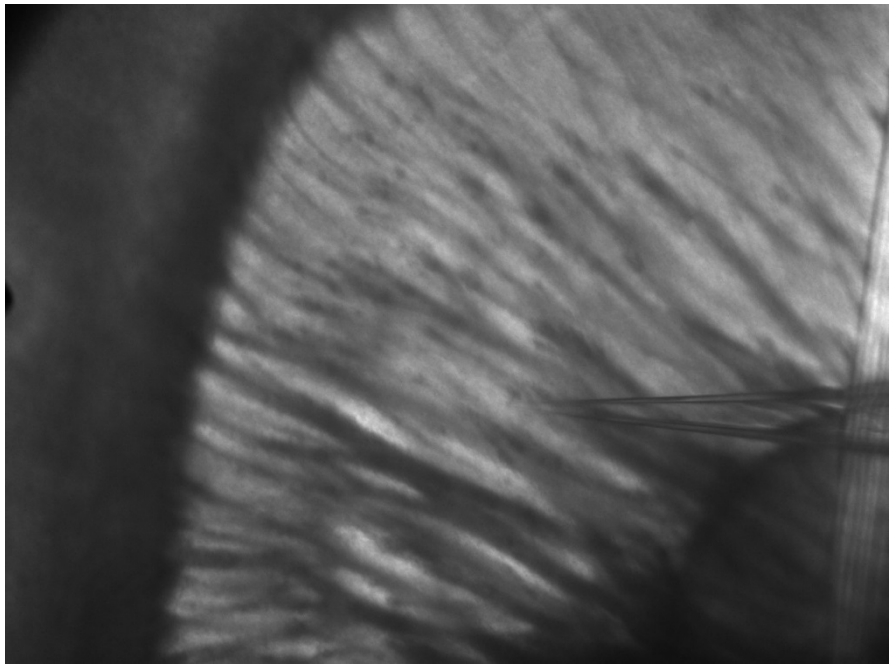
# Materials and Methods Ctd.

- Data Collection
  - Transgenic mice brain slices
    - Npas1-Cre;D2-GFP
  - Whole Cell Patch Clamping
    - Fluorescent Dye (Alexa 647 hydrazide)
  - Surrounding GPe axons
    - YFP+ (visualized in the 488 nm range)
    - Protein Fluoresce
  - Confocal Microscopy



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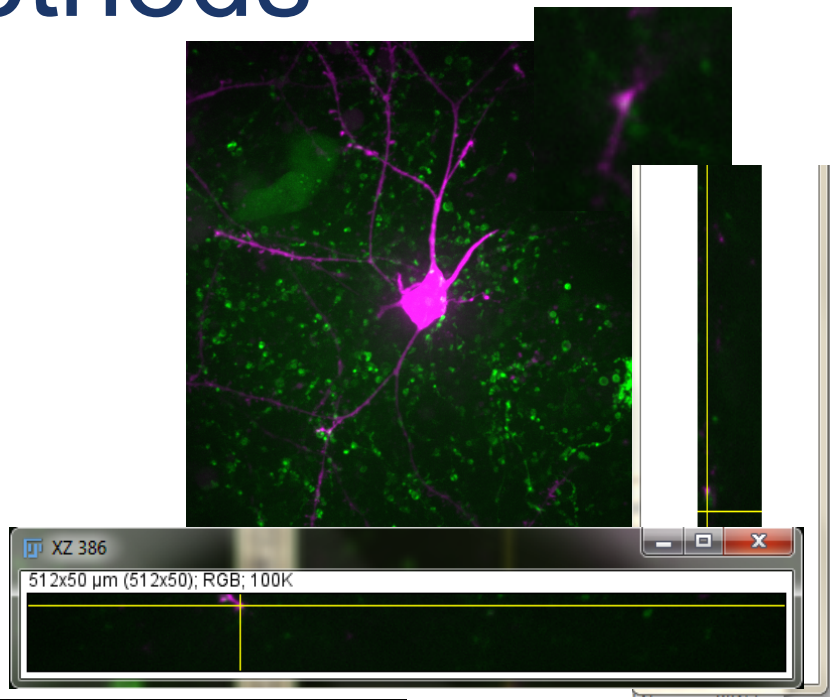
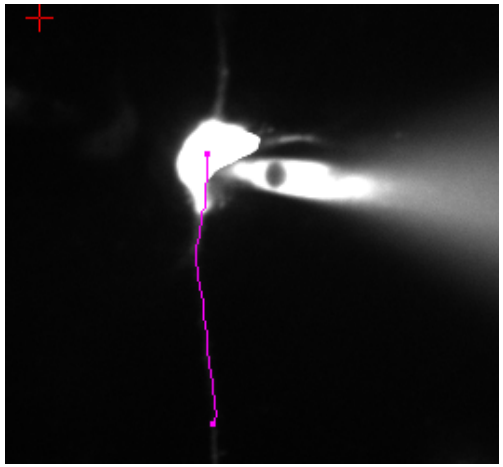
# Materials and Methods

- Fiji ImageJ software
- Pallidostriatal contacts
  - Between SPN dendrites and axons of the GPe
  - Verified in the orthogonal plane
- Contacts measured via two methods
  - Euclidian distance calculated
  - Trace of dendrite to soma



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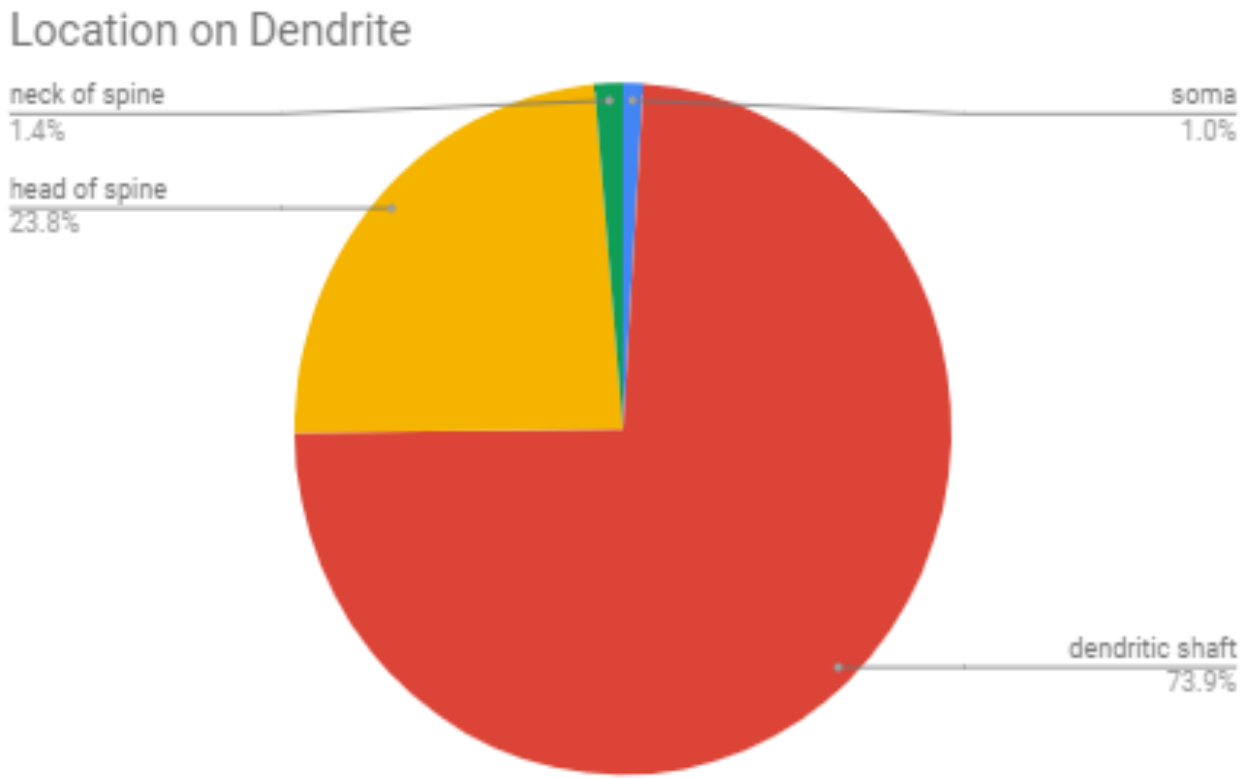
# General Location of Synapses

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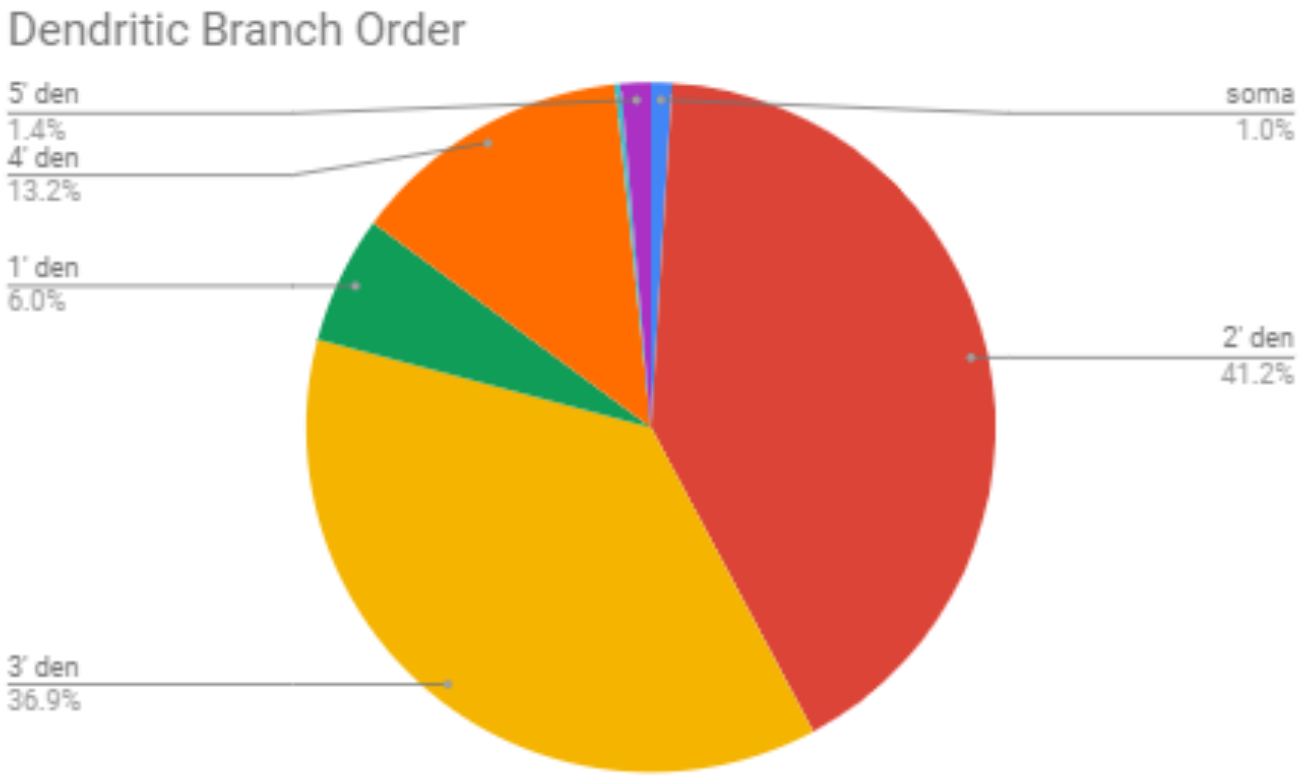
# General Branch Order and Location of Synapses

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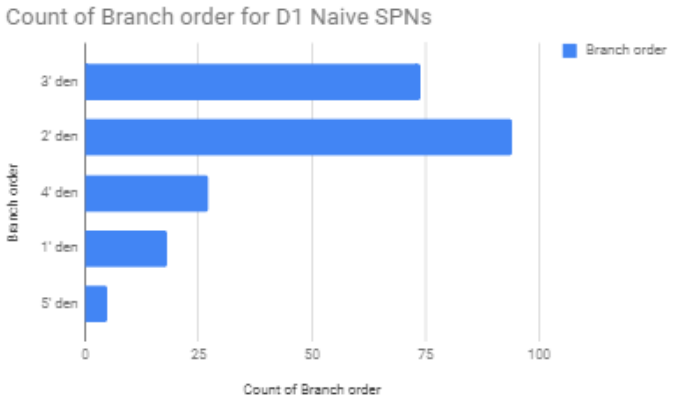
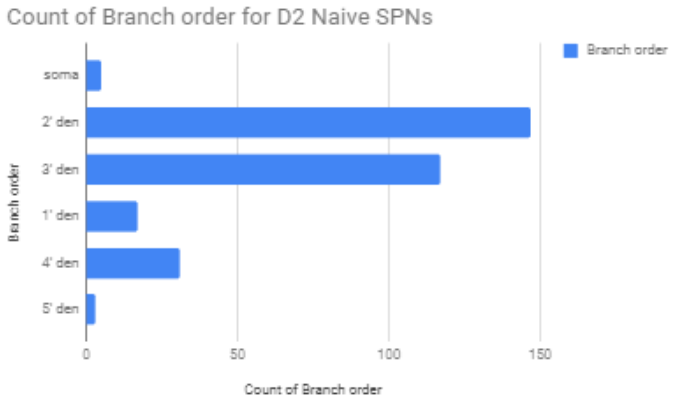
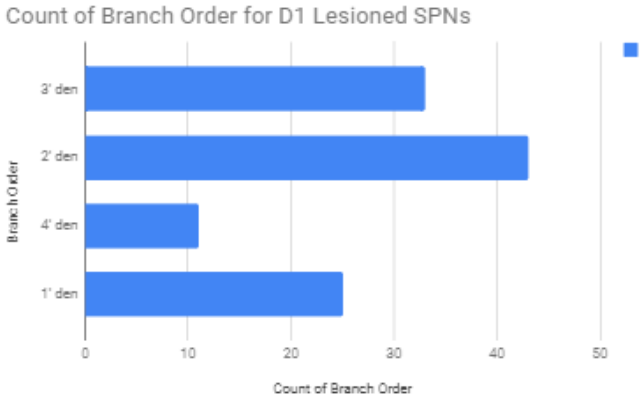
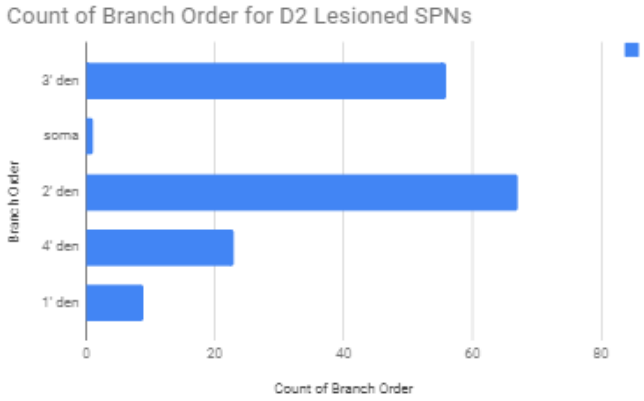
# Branch Order for Each Group of SPNs

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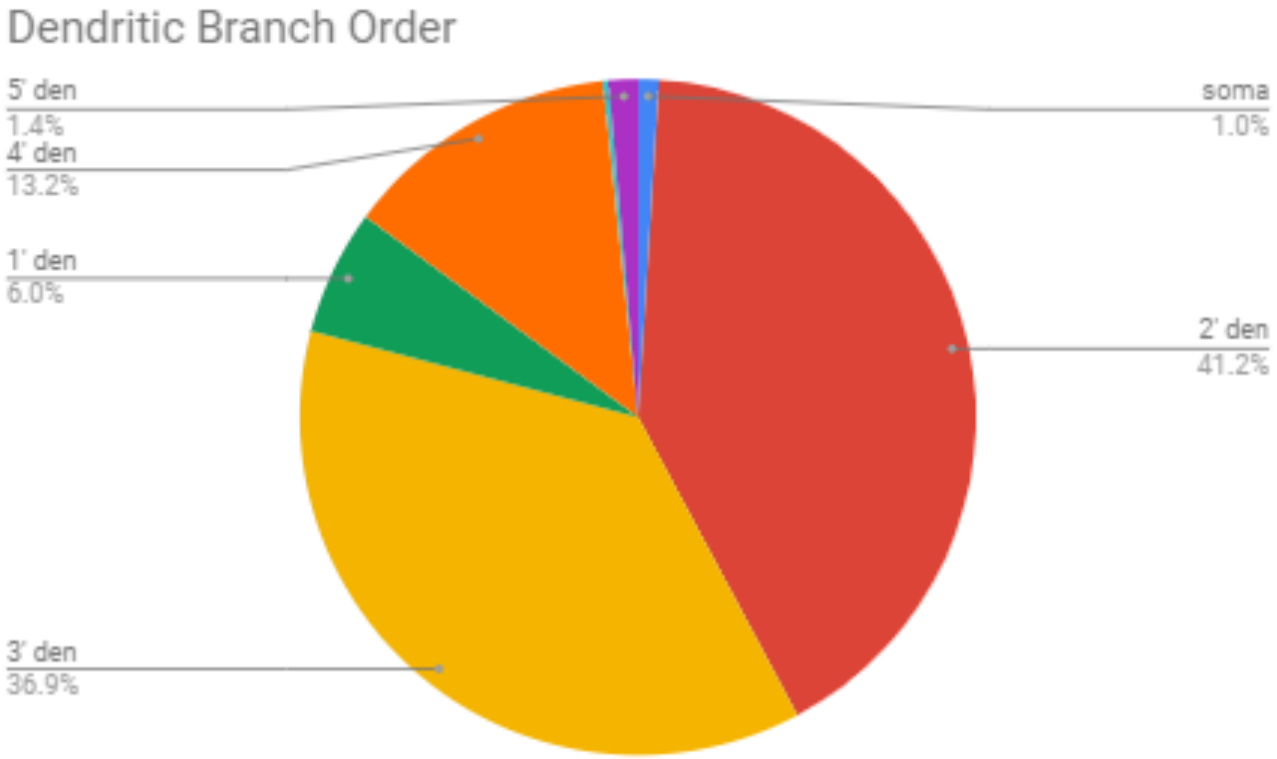
# General Branch Order and Location of Synapses

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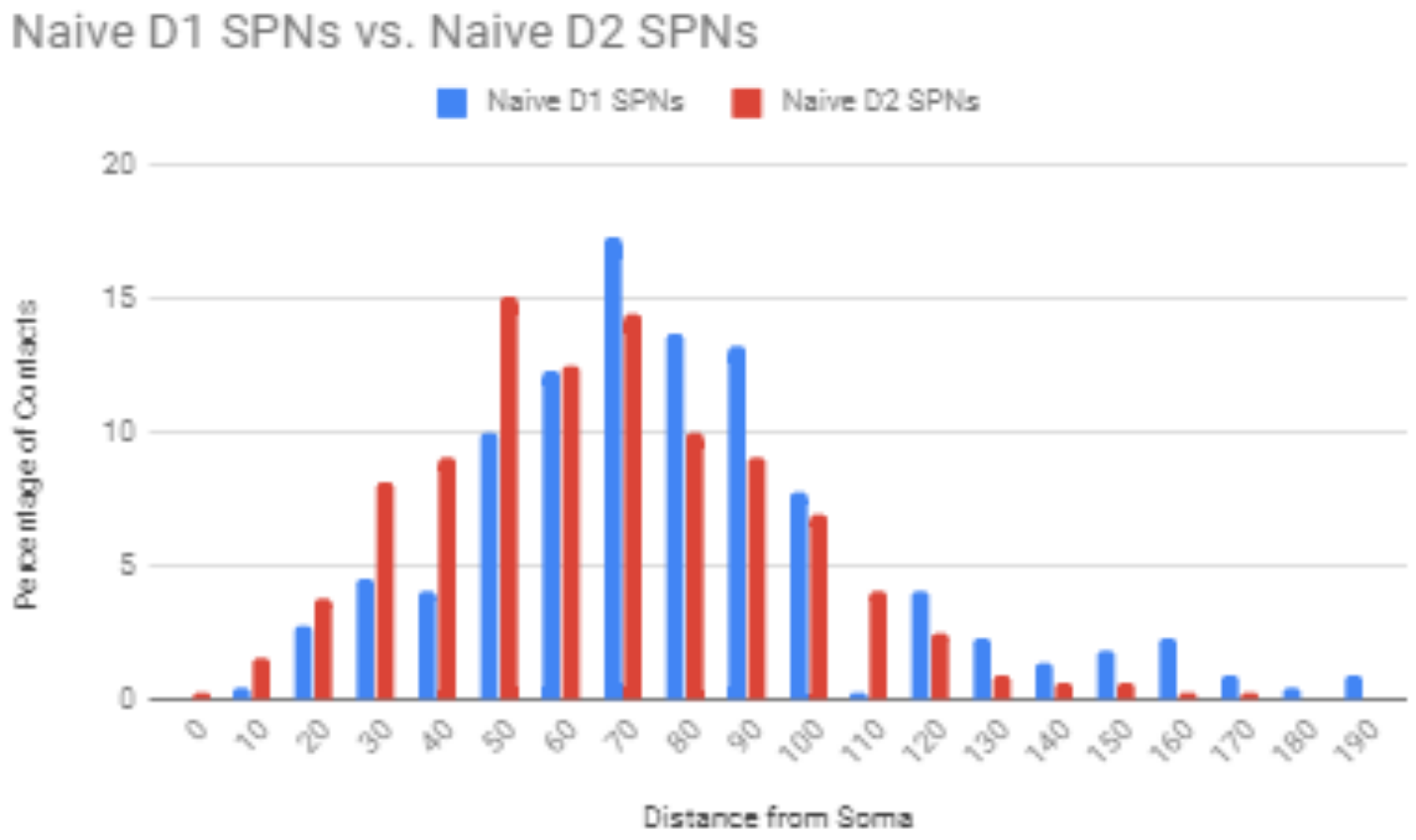
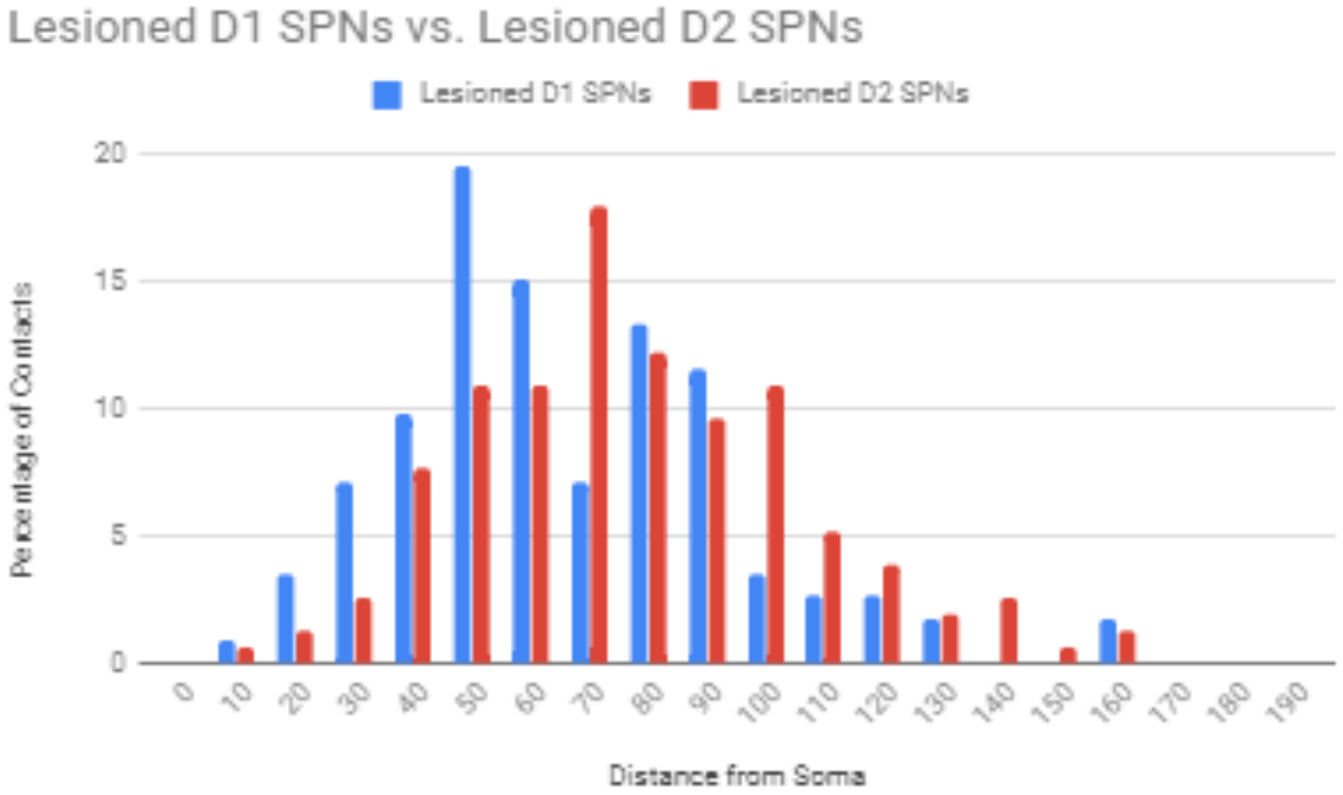
# Contacts per Cell

| | D1 SPNs | D2 SPNs |
|---|---|---|
| Naive | 6.9 contacts | 7.1 contacts |
| Lesioned | 6.3 contacts | 7.1 contacts |

# Naïve Group Projections



# Lesioned Group Projections

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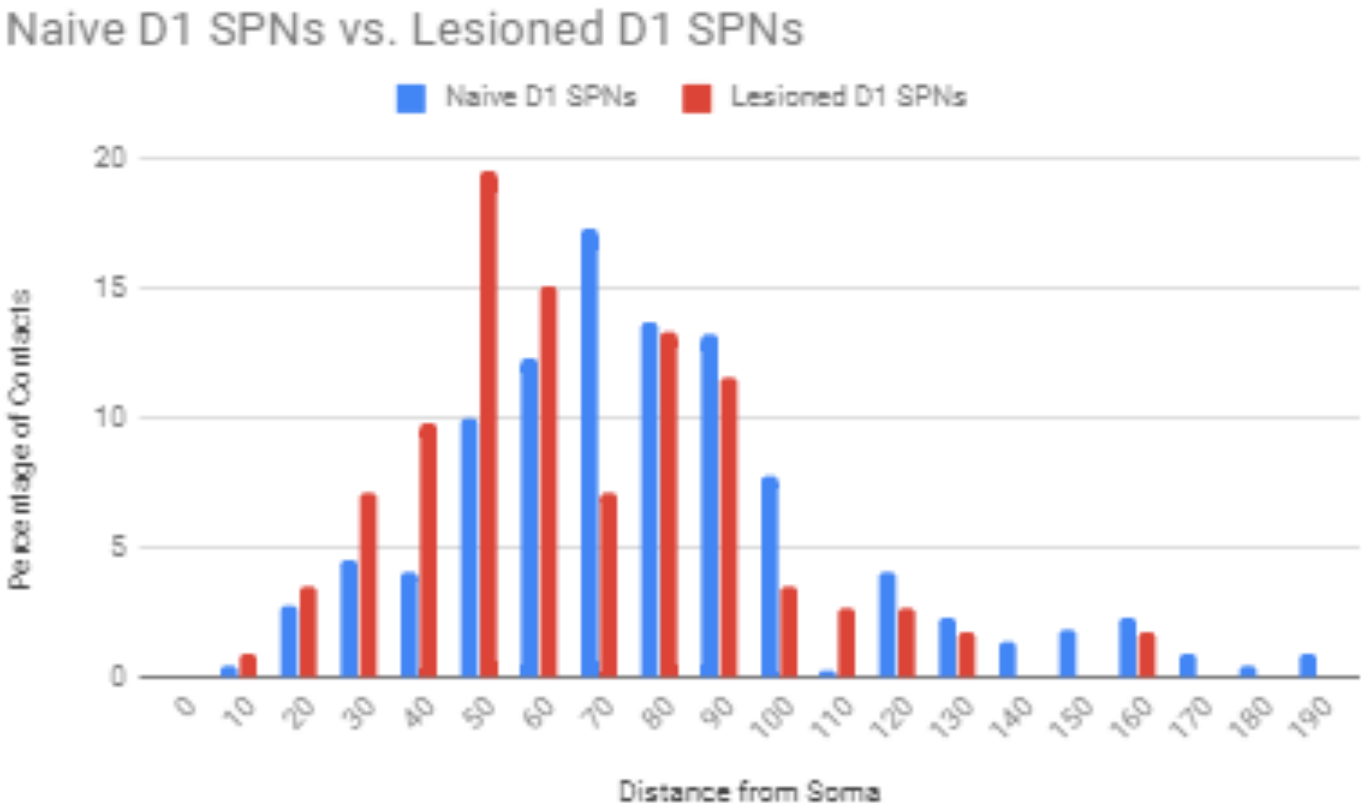
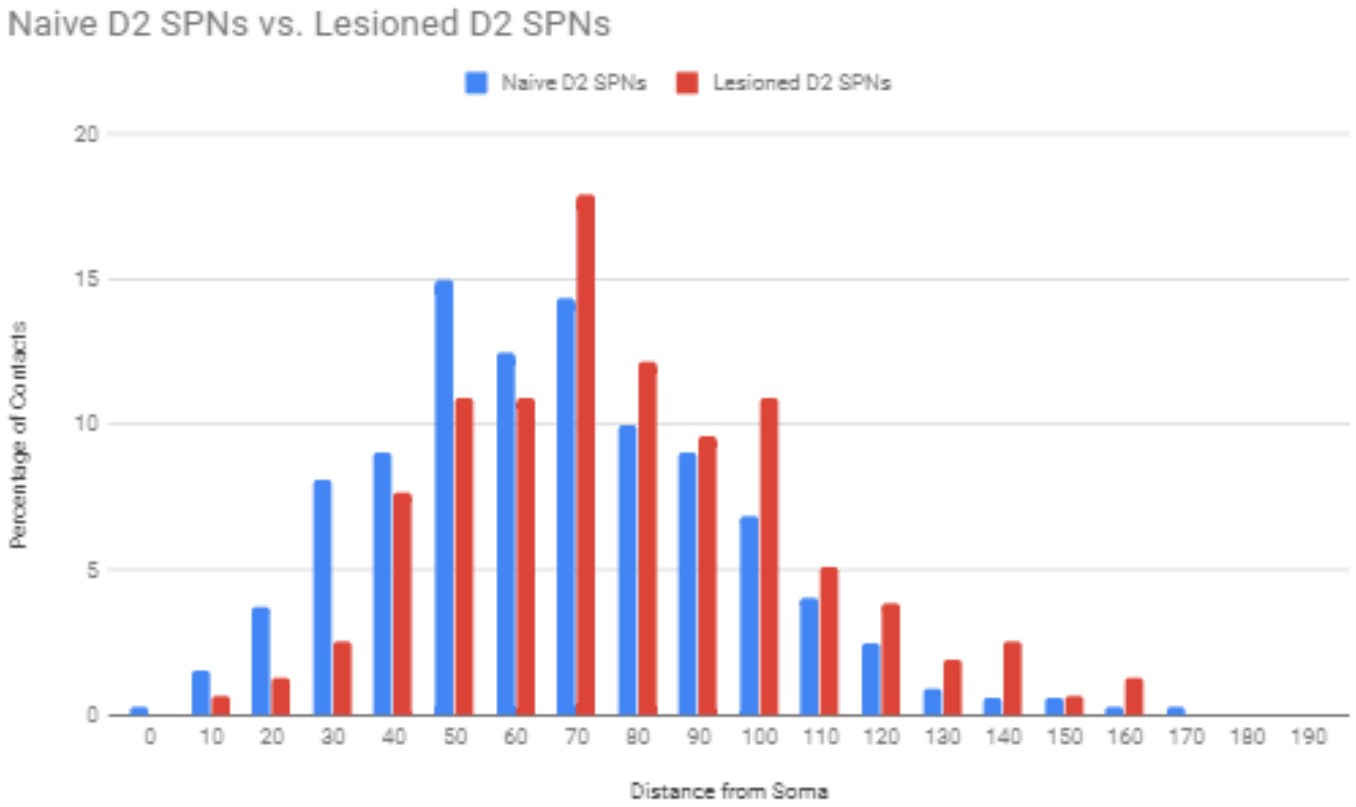
# Weakened Projections of D1 SPNs



# Stronger Projections of D2 SPNs

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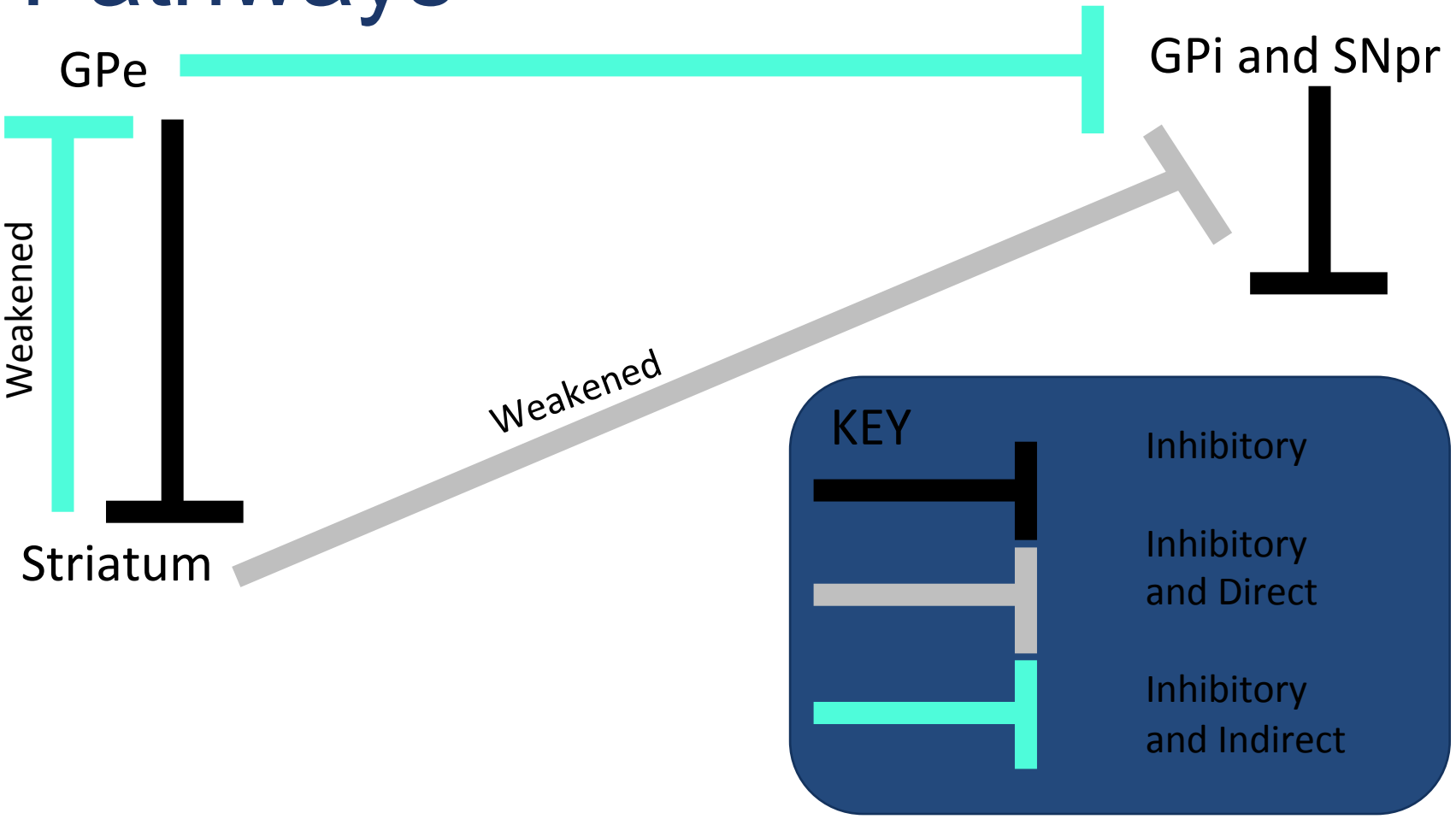
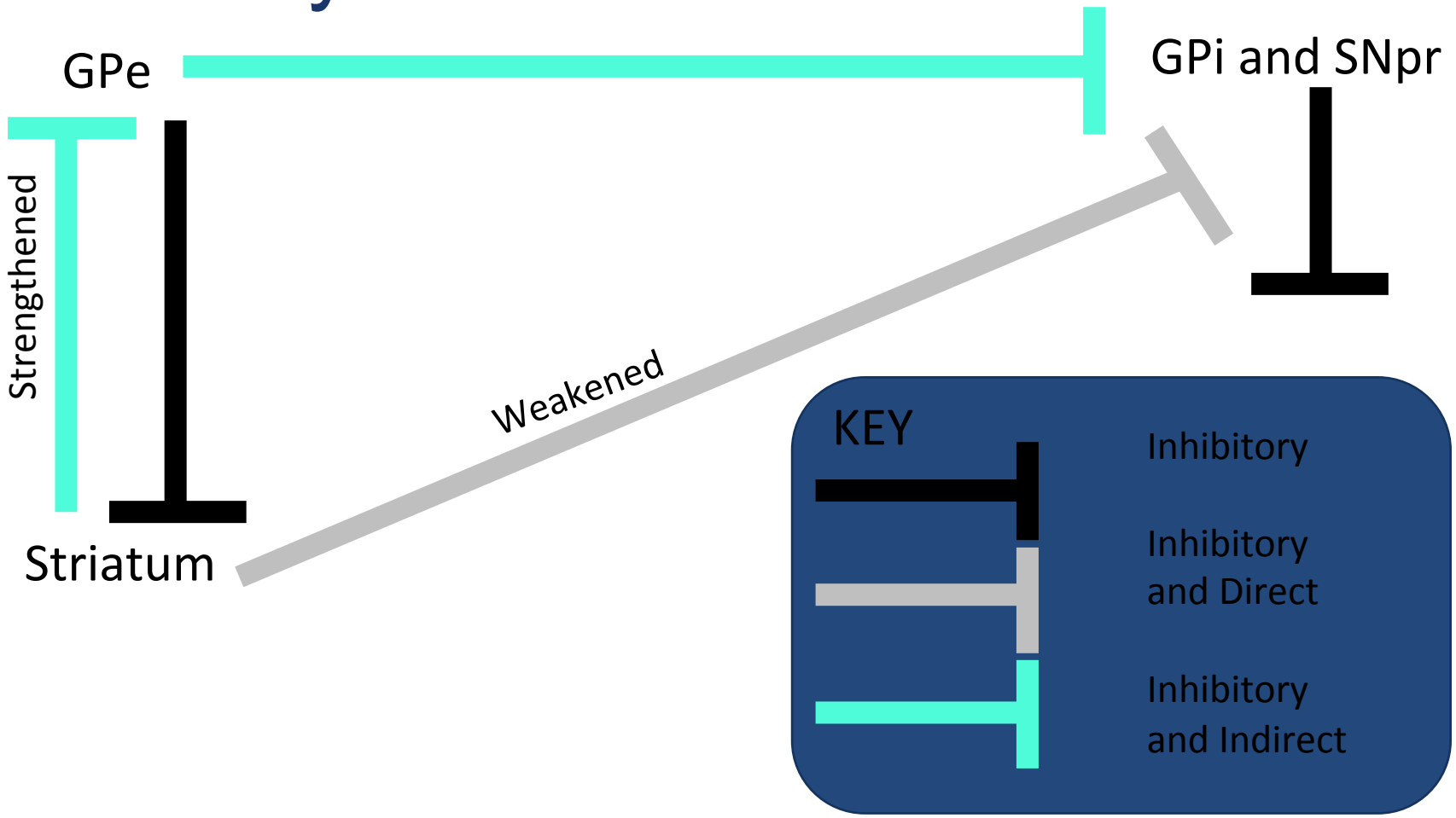
# Direct Striatal and Pallidal Pathways



# Indirect Striatal and Pallidal Pathways



# Summary

- Most synapses occurred on 2’ and 3’ dendrites
  - Inhibits cortical excitatory input
- Most synapses occurred on the dendritic shaft
- The frequency of synapses was unaffected.
- The projections of the iSPNs are increased in the lesioned model.
  - Further inhibits cortical excitatory input
- The projections of the dSPNs are diminished in the lesioned model.

# Acknowledgements

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